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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/801,982	03/16/2004	Marianna Goldrick	6545	2505

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EXAMINER	
LU, FRANK WEI MIN	
ART UNIT	**PAPER NUMBER**
1634	
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09/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/801,982	GOLDRICK, MARIANNA	
	Examiner	Art Unit	
	Frank W. Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14,16-22 and 25-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14,16-22 and 25-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicant's response to the office action filed on June 27, 2007 has been entered. The claims pending in this application are claims 1-14, 16-22, and 25-34. Rejection and/or objection not reiterated from the previous office action are hereby withdrawn in view of the amendment filed on June 27, 2007.

Claim Objections

2. Claim 25 is objected to because of the following informality: the word "would" in line 2 should be deleted.

Appropriate correction is required.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-4, 7, 8, 10, 11, 14-18, 28, and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garvin (US 2003/0170669, published on September 11, 2003 and priority date: April 11, 2000) in view of Korfhage *et al.,* (US Patent No. 6,872,818 B2, priority date: January 25, 2001).

Regarding claims 1-3, Garvin teaches a method of obtaining a leukocyte lysate comprising RNA comprising fractionating leukocytes from whole blood using a leukocyte depletion matrix (ie., the filter media) and lysing the fractionated leukocytes to obtain a lysate comprising RNA as recited in claim 1 wherein the leukocytes are comprised on the matrix at the time they are lysed as recited in claim 2 (see abstract, page 1, [0006], [0009] and [0018]) and the leukocyte comprising matrix is stored for a period of time (ie., the time between step (a) and step (c) in the method of Garvin) prior to lysis of the leukocytes as recited in claim 3 (ie., page 1, [0009]).

Regarding claims 4, 7, and 8, Garvin teaches that the fractionated leukocytes are contacted with a lysis solution (ie., the solution comprising a chaotopic agent) as recited in claim 4 wherein the lysis solution contains a chaotropic agent as recited in claim 7 and the chaotropic agent is a guanidinium salt as recited in claim 8 (see page 1, [0018]).

Regarding claims 10, 11, and 14, since it is known that guanidinium hydrochloride is a ribonuclease inhibitor, Garvin teaches that the lysis solution comprises a ribonuclease inhibitor (ie., guanidinium hydrochloride) as recited in claim 10, further comprising extracting the RNA from the lysate as recited in claim 11 and further comprising extracting RNA and DNA from the lysate as recited in claim 14 (see page 1, [0018]).

Regarding claim 29, Garvin teaches fractionating leukocytes from blood by capturing them with a leukocyte depletion matrix (ie., the filter media), lysing the fractionated leukocytes to produce a lysate, and isolating RNA from the lysate (see abstract, page 1, [0006], [0009] and [0018]).

Garvin does not disclose treating the fractionated leukocytes with an RNA

preservation composition comprising a salt that infiltrates the leukocytes and increases the half-life of the RNA compared to the RNA in cells not treated with the preservation composition and reduces the gDNA contamination of the subsequent lysate compared to fractionated leukocytes that were not treated with the preservation composition as recited in claims 1 and 28 wherein the salt is a sulfate salt as recited in claim 16, the salt is ammonium sulfate as recited in claim 17, and the final salt concentration in the preservation composition is between 10 g/100 ml and a saturating concentration as recited in claim 18. However, Garvin does teach fractionating leukocytes from blood by capturing them with a leukocyte depletion matrix, lysing the fractionated leukocytes to produce a lysate, and isolating RNA from the lysate as recited in claim 28 (see abstract, page 1, [0006], [0009] and [0018]).

Regarding claims 1, 16, 17 and 28, since Korfhage *et al.*, teach to use ammonium sulfate to mitigate or neutralize inhibitory effects of certain molecules that interfere with RNA function or to reduce the detrimental effects of some agents on RNA activity (see abstract and column 2, lines 1-10), Korfhage *et al.*, disclose an RNA preservation composition comprising a salt (ie., ammonium sulfate) that infiltrates the leukocytes and increases the half-life of the RNA compared to the RNA in cells not treated with the preservation composition and reduces the gDNA contamination of the subsequent lysate (ie., by decreasing RNA degradation) compared to fractionated leukocytes that were not treated with the preservation composition as recited in claims 1 and 28 wherein the salt is a sulfate salt as recited in claim 16 and the salt is ammonium sulfate as recited in claim 17.

Regarding claim 18, Korfhage *et al.*, teach that the final salt concentration (ie., ammonium sulfate) in the preservation composition is between 10 g/100 ml and a saturating concentration (below 20 g/100 ml) (see column 1, lines 56-60).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the methods recited in claims 1 and 28 by treating the fractionated leukocytes with an RNA preservation composition comprising a salt that infiltrates the leukocytes and increases the half-life of the RNA compared to the RNA in cells not treated with the preservation composition and reduces the gDNA contamination of the subsequent lysate compared to fractionated leukocytes that were not treated with the preservation composition and contacting the RNA preservation with the matrix in view of the prior art of Garvin and Korfhage *et al.*. One having ordinary skill in the art would have been motivated to do so because the Korfhage *et al.*, teach to use ammonium sulfate to mitigate or neutralize inhibitory effects of certain molecules that interfere with RNA function or to reduce the detrimental effects of some agents on RNA activity (see abstract and column 2, lines 1-10) so that the half-life of the RNA is increased and the genomic DNA contamination is reduced (ie., by decreasing RNA degradation). One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to perform the methods recited in claims 1 and 28 by treating the fractionated leukocytes with an RNA preservation composition comprising ammonium sulfate and contacting the RNA preservation with the matrix in order to increase the half-life of the RNA and reduce the genomic DNA contamination.

5. Claims 1-4, 7, 8, 10, 11, 14-23, 28, and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garvin in view of Lader (US Patent No. 6,204,375 B1, published on March 20, 2001).

Regarding claims 1-3, Garvin teaches a method of obtaining a leukocyte lysate comprising RNA comprising fractionating leukocytes from whole blood using a leukocyte depletion matrix (ie.; the filter media) and lysing the fractionated leukocytes to obtain a lysate comprising RNA as recited in claim 1 wherein the leukocytes are comprised on the matrix at the time they are lysed as recited in claim 2 (see abstract, page 1, [0006], [0009] and [0018]) and the leukocyte comprising matrix is stored for a period of time (ie., the time between step (a) and step (c) in the method of Garvin) prior to lysis of the leukocytes as recited in claim 3 (ie., page 1, [0009]).

Regarding claims 4, 7, and 8, Garvin teaches that the fractionated leukocytes are contacted with a lysis solution (ie., the solution comprising a chaotopic agent) as recited in claim 4 wherein the lysis solution contains a chaotropic agent as recited in claim 7 and the chaotropic agent is a guanidinium salt as recited in claim 8 (see page 1, [0018]).

Regarding claims 10, 11, and 14, since it is known that guanidinium hydrochloride is a ribonuclease inhibitor, Garvin teaches that the lysis solution comprises a ribonuclease inhibitor (ie., guanidinium hydrochloride) as recited in claim 10, further comprising extracting the RNA from the lysate as recited in claim 11 and further comprising extracting RNA and DNA from the lysate as recited in claim 14 (see page 1, [0018]).

Regarding claim 29, Garvin teaches fractionating leukocytes from blood by

capturing them with a leukocyte depletion matrix (ie., the filter media), lysing the fractionated leukocytes to produce a lysate, and isolating RNA from the lysate (see abstract, page 1, [0006], [0009] and [0018]).

Garvin does not disclose treating the fractionated leukocytes with an RNA preservation composition comprising a salt that infiltrates the leukocytes and increases the half-life of the RNA compared to the RNA in cells not treated with the preservation composition and reduces the gDNA contamination of the subsequent lysate compared to fractionated leukocytes that were not treated with the preservation composition as recited in claims 1 and 28 wherein the salt is a sulfate salt as recited in claim 16, the salt is ammonium sulfate as recited in claim 17, the final salt concentration in the preservation composition is between 10 g/100 ml and a saturating concentration as recited in claim 18, wherein the salt is present in the preservation composition at a final concentration of between 20 g/100 ml and the saturating concentration of the salt as recited in claim 19, wherein the salt is present in the preservation composition at a final concentration of between 30 g/100 ml and 80 g/100 ml as recited in claim 20, wherein the RNA preservation composition comprises at least two salts as recited in claim 21 and the total salt concentration is present in the preservation composition at a final concentration of between 20 g/100 ml and 100 g/100 ml as recited in claim 22. However, Garvin does teach fractionating leukocytes from blood by capturing them with a leukocyte depletion matrix, lysing the fractionated leukocytes to produce a lysate, and isolating RNA from the lysate as recited in claim 28 (see abstract, page 1, [0006], [0009] and [0018]).

Regarding claims 1, 16, 17 and 28, since Lader teaches to use an RNA preservation medium comprising ammonium sulfate in order to protect the RNA from

nucleases (see column 3, fourth paragraph), Lader discloses an RNA preservation composition comprising a salt (ie., ammonium sulfate) that infiltrates the leukocytes and increases the half-life of the RNA compared to the RNA in cells not treated with the preservation composition and reduces the gDNA contamination of the subsequent lysate (ie., by decreasing RNA degradation) compared to fractionated leukocytes that were not treated with the preservation composition as recited in claims 1 and 28 wherein the salt is a sulfate salt as recited in claim 16 and the salt is ammonium sulfate as recited in claim 17.

Regarding claims 18-22, Lader teaches that the final salt concentration in the preservation composition is between 10 g/100 ml and a saturating concentration as recited in claim 18, the salt is present in the preservation composition at a final concentration of between 20 g/100 ml and the saturating concentration of the salt as recited in claim 19, the salt is present in the preservation composition at a final concentration of between 30 g/100 ml and 80 g/100 ml as recited in claim 20, the RNA preservation composition comprises at least two salts as recited in claim 21 and the total salt concentration is present in the preservation composition at a final concentration of between 20 g/100 ml and 100 g/100 ml as recited in claim 22 (see column 3-5).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the methods recited in claims 1 and 28 by treating the fractionated leukocytes with an RNA preservation composition comprising a salt that infiltrates the leukocytes and increases the half-life of the RNA compared to the RNA in cells not treated with the preservation composition and reduces the gDNA contamination of the subsequent lysate compared to fractionated

leukocytes that were not treated with the preservation composition and contacting the RNA preservation with the matrix in view of the prior art of Garvin and Lader. One having ordinary skill in the art would have been motivated to do so because Lader teaches to use an RNA preservation medium comprising ammonium sulfate in order to protect the RNA from nucleases (see column 3, fourth paragraph) so that the half-life of the RNA is increased and the genomic DNA contamination is reduced (ie., by decreasing RNA degradation). One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to perform the methods recited in claims 1 and 28 by treating the fractionated leukocytes with an RNA preservation composition comprising ammonium sulfate and contacting the RNA preservation with the matrix in order to increase the half-life of the RNA and reduce the genomic DNA contamination.

6. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Garvin in view of Korfhage *et al.*, as applied to claims 1-4, 7, 8, 10, 11, 14-18, 28, and 29 above or Garvin in view of Lader as applied to claims 1-4, 7, 8, 10, 11, 14-23, 28, and 29, and further in view of Rutter *et al.*, (US Patent No. 4,652,525, published on March 24, 1987).

The teachings of Garvin, Korfhage *et al.*, and Lader have been summarized previously, *supra*.

Garvin, Korfhage *et al.*, and Lader do not disclose that the guanidinium salt is guanidinum thiocyanate as recited in claim 9.

Rutter *et al.*, teach to isolate mRNA using guanidinum thiocyanate (see column 10, last paragraph).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 9 wherein the guanidinum salt is guanidinum thiocyanate in view of the prior art of Garvin, Korfhage *et al.*, or Lader and Rutter *et al.*. One having ordinary skill in the art would have been motivated to do so because, comparing with guanidinum hydrochloride, guanidinum thiocyanate is a more effective denaturing agent to inhibit RNase (see column 10, last paragraph). One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to perform the method recited in claim 9 using guanidinum thiocyanate in order to more effectively inhibit RNase during the process for isolating RNA.

7. Claims 5 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garvin in view of Korfhage *et al.*, and Rutter *et al.*, as applied to claims 1-4, 7-11, 14-18, 28, and 29 above or Garvin in view of Lader and Rutter *et al.*, as applied to claims 1-4, 7-11, 14-23, 28, and 29, and further in view of Ala-Kokko *et al.*, (US Patent No. 5,045,449, published on September 3, 1991).

The teachings of Garvin, Korfhage *et al.*, Lader and Rutter *et al.*, have been summarized previously, *supra*.

Garvin, Korfhage *et al.*, Lader and Rutter *et al.*, do not disclose that the lysis solution comprises a detergent wherein the detergent is Triton X-100, Tween-20, SDS (sodium dodecyl sulfate), sarcosyl, or deoxycholic acid as recited in claims 5 and 6.

Ala-Kokko *et al.*, teach to isolate total RNA using a lysis solution comprising sarcosyl and guanidinum thiocyanate (see column 5, third paragraph).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the methods recited in claims 5 and 6 wherein the lysis solution further comprises a detergent such as sarcosyl in view of the prior art of Garvin, Korfhage *et al.*, or Lader, Rutter *et al.*, and Ala-Kokko *et al.*. One having ordinary skill in the art would have been motivated to do so because addition of sarcosyl into a lysis solution comprising guanidinum thiocyanate would enhance to lyse the cells during the process for isolating RNA (see column 5, third paragraph). One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to perform the method recited in claims 5 and 6 by adding sarcosyl into a lysis solution comprising guanidinum thiocyanate.

8. Claims 12, 13, and 25-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garvin in view of Korfhage *et al.*, as applied to claims 1-4, 7, 8, 10, 11, 14-18, 28, and 29 above or over Garvin in view of Lader as applied to claims 1-4, 7, 8, 10, 11, 14-23, 28, and 29, and further in view of Maniatis *et al.*, (Molecular Cloning: A Laboratory Manual, pages 191-193, 1982).

The teachings of Garvin, Korfhage *et al.*, and Lader have been summarized previously, *supra*.

Garvin, Korfhage *et al.*, and Lader do not disclose that extracting the RNA is performed via an organic extraction as recited in claim 12 wherein the organic extraction is a phenol/chloroform extraction as recited in claim 13 and do not disclose extracting the lysate with an organic solution to form organic and aqueous phases and separating the organic and aqueous phases as recited in claim 26, and extracting the lysate with an

organic solution to form organic and aqueous phases and separating the organic and aqueous phases as recited in claim 27. However, Garvin does teach fractionating leukocytes from blood by capturing them with a leukocyte depletion matrix, lysing the fractionated leukocytes to produce a lysate and isolating RNA as recited in claim 26 (see abstract, page 1, [0006], [0009] and [0018]). Since Garvin in view of Korfhage *et al.*, or Lader teach claims 1 and 28 (see above rejection), Garvin in view of Korfhage *et al.*, or Lader disclose that the extracted RNA has less DNA contamination than would RNA extracted from fractionated leukocytes that were not treated with the RNA preservation medium as recited in claim 25 and fractionating leukocytes from blood by capturing them with a leukocyte depletion matrix, treating the fractionated leukocytes with an RNA preservation composition comprising a salt that infiltrates the leukocytes, increasing the half-life of the RNA, lysing the fractionated leukocytes to produce a lysate and isolating RNA as recited in claim 27.

Maniatis *et al.*, teach to extract RNA via phenol/chloroform (see page 192).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the methods recited in claims 12, 13, 26, and 27 by extracting the RNA via phenol/chloroform in view of the prior art of Garvin, Korfhage *et al.*, or Lader and Maniatis *et al.*. One having ordinary skill in the art would have been motivated to do so because Garvin suggests to isolate RNA using a known manner (see page 1, [0017] and RNA isolation method taught by Maniatis *et al.*, is well known method for isolating RNA. One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of

success to perform the method recited in claims 12, 13, 26, and 27 using RNA isolation method taught by Maniatis *et al.*.

9. Claims 30-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over in view of Korfhage *et al.*, as applied to claims 1-4, 7, 8, 10, 11, 14-18, 28, and 29 above or over Garvin in view of Lader as applied to claims 1-4, 7, 8, 10, 11, 14-23, 28, and 29, and further in view of Warrington *et al.*, (US Patent No. 7,108,969 B1, filed on September 10, 2001).

The teachings of Garvin, Korfhage *et al.*, and Lader have been summarized previously, *supra*.

Garvin, Korfhage *et al.*, and Lader do not disclose further comprising assaying for the presence or quantity of one or more RNAs in the lysate as recited in claim 30 wherein assaying comprises a Northern blot, RNase protection assay, hybridization reaction, microarray analysis, or reverse transcriptase-polymerase chain reaction analysis as recited in claim 31 wherein assaying comprises a reverse transcriptase-polymerase chain reaction further defined as real-time RT-PCR or endpoint RT-PCR as recited in claim 32, assaying comprises a microarray analysis as recited in claim 33 and the microarray analysis comprises the use of a cDNA array, spotted oligonucleotide array, or in-situ synthesized oligonucleotide array as recited in claim 34.

Warrington *et al.*, teach that the quality and quantity of isolated RNA is examined by RT-PCR and the microarray analysis using spotted oligonucleotide array (see column 13, lines 57-67 and column 14).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in

the art at the time the invention was made to have assayed for the presence or quantity of one or more RNAs in the lysate as recited in claim 30 wherein assaying comprises microarray analysis or reverse transcriptase-polymerase chain reaction analysis as recited in claim 31 wherein assaying comprises a reverse transcriptase-polymerase chain reaction further defined as real-time RT-PCR as recited in claim 32, assaying comprises a microarray analysis as recited in claim 33 and the microarray analysis comprises the use of a spotted oligonucleotide array as recited in claim 34 in view of the prior art of Garvin, Korfhage *et al.*, or Lader and Warrington *et al.*. One having ordinary skill in the art would have been motivated to do so because Garvin suggests that isolated RNA is used for different purposes such as population based genetic studies (see column 2, [0020]) and Warrington *et al.*, teach that the quality and quantity of isolated RNA is examined by RT-PCR and the microarray analysis using spotted oligonucleotide array (see column 13, lines 57-67 and column 14). One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to perform RT-PCR and the microarray analysis using spotted oligonucleotide array in order to examine quality and quantity of the isolated RNA.

Response to Arguments

In page 11, last paragraph bridging to page 12, last paragraph of applicant's remarks, applicant argues that: (1) "[A]pplicant submits that any combination of Garvin with Rutter *et al.*, Ala-Kokko *et al.*, Maniatis *et al.*, Korthage *et aL*, Lader, or Warrington *et al.*, as cited above, does not render the subject matter set forth by the pending claims obvious, in part, because the combination of prior art references fails the 'objective reach of the claims' test regarding 'fractionating leukocytes from whole blood using a

leukocyte depletion matrix; treating the fractionated leukocytes with an RNA preservation composition comprising a salt that infiltrates the leukocytes and (i) increases the half-life of the RNA compared to the RNA in cells not treated with the preservation composition and (ii) reduces the gDNA contamination of the subsequent lysate compared to fractionated leukocytes that were not treated with the preservation composition; and lysing the fractionated leukocytes to obtain a lysate comprising RNA and reduced gDNA contamination compared to a lysate of fractionated leukocytes that were not treated with the RNA preservation composition'."; and (2) "[A]pplicant notes that although there is a vast amount of knowledge about general relationships in the chemical and biochemical arts, chemistry and biochemistry are still largely empirical, and there is often great difficulty in predicting precisely how a given compound will behave. 'Fractionating leukocytes from whole blood using a leukocyte depletion matrix; treating the fractionated leukocytes with an RNA preservation composition comprising a salt that infiltrates the leukocytes and (i) increases the half-life of the RNA compared to the RNA in cells not treated with the preservation composition and (ii) reduces the gDNA contamination of the subsequent lysate compared to fractionated leukocytes that were not treated with the preservation composition; and lysing the fractionated leukocytes to obtain a lysate comprising RNA and reduced gDNA contamination compared to a lysate of fractionated leukocytes that were not treated with the RNA preservation composition' is outside of the objective reach of any combination of art cited".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection because there are motivations to combine Garvin with

Rutter *et al.*, Ala-Kokko *et al.*, Maniatis *et al.*, Korthage *et aL,* Lader, or Warrington *et al.*, (see above rejection).

Conclusion

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. No claim is allowed.

12. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571)272-0735.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

August 29, 2007

FRANK LU
PRIMARY EXAMINER